Objectives

1) Compare and contrast live attenuated vaccines and inactivated vaccines
2) Identify possible drug interactions with vaccines
3) Differentiate between valid and not valid contraindications and/or precautions to use of a given vaccine
4) Recommend appropriate vaccines, including number of doses and time periods, for a patient based on age and/or risk factors
5) Choose an appropriate therapy for the prevention or treatment of influenza, given a patient case

Key terms

- **Immunity**
  - Ability of the human body to tolerate the presence of material indigenous to the human body and to eliminate foreign material
- **Passive immunity**
  - Gained immunity from products produced by an animal or human and transferred to another human
- **Active immunity**
  - Immunity produced by a person’s own immune system after exposure to an antigen
- **Antigen**
  - Live or inactivated substance capable of producing an immune response
- **Antibody**
  - Protein molecules produced by B lymphocytes to help eliminate an antigen

Types of vaccines

- **Live attenuated vaccines**
  - **Source**
  - Number of doses required
  - Because this type of vaccine contains a live virus, caution must be used in immunocompromised patients
  - Vaccine failure will occur if antibodies to the virus or bacteria are present
- **Inactivated vaccines**
  - **Source**
  - Number of doses required
  - Booster shots are required as antibody concentrations will diminish over time
- **Polysaccharide vaccines**
  - **Source**
  - Polysaccharide chain acts as an antigen, eliciting an immune response
  - Booster shots do not offer an advantage to increasing immunity
- **Recombinant vaccines**
  - **Source**
  - Examples of genetic engineering
    - Removal of the ability to cause disease
    - Reproduction of the organism is limited to a certain cell type
    - Replication and production of antigen
- **Classification of common vaccines**
Vaccine Basics

- **Adverse Reactions**
  - Three types
    - Local reactions: pain, swelling, redness at injection site
    - Systemic: fever, malaise, headache, anorexia
    - Anaphylactic reactions
  - Special process for reporting adverse reactions through the Vaccine Adverse Event Reporting System (VAERS)
    - Form available at [www.vaers.hhs.gov](http://www.vaers.hhs.gov)

- **Allergies**
  - Both the vaccine and the vaccine component are important to obtain from patient (or guardian)
  - If a patient has anaphylaxis to any vaccine or component, contraindication to administer
  - List of common allergies and vaccines ***NOT*** to be given

<table>
<thead>
<tr>
<th>Allergy</th>
<th>Vaccines contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eggs</td>
<td>Influenza vaccine, yellow fever</td>
</tr>
<tr>
<td>Gelatin</td>
<td>Varicella, MMR</td>
</tr>
<tr>
<td>Neomycin</td>
<td>MMR, inactivated polio vaccine, varicella, vaccinia</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>Inactivated polio vaccine, vaccinia</td>
</tr>
<tr>
<td>Latex</td>
<td>All vaccines; Vials containing vaccine to be administered should use a vial without natural rubber</td>
</tr>
</tbody>
</table>

- **Contraindications**
  - Valid contraindications
    - Vaccines include intranasal flu, MMR, PPV, rabies, PO typhoid, vaccinia, varicella, yellow fever
    - Contraindication may extend beyond individual dependent on vaccine
      - Household contacts: live flu vaccine, vaccinia
      - Family history: varicella
  - Vaccines include
    - MMR and varicella – pregnancy should be avoided for 4 weeks after immunization
    - Intranasal flu and vaccinia
    - Inactivated polio vaccine and Hepatitis A – may be given to those at high risk
    - Japanese encephalitis – if travelling to endemic country, weigh risk vs benefit
    - Yellow fever – Should try to avoid travel to endemic country until pregnancy complete; weigh risk vs benefit; should obtain waiver for vaccine prior to travel
    - HPV and typhoid – not contraindicated but no data exist on safety
• Contraindications concerned with diphtheria/tetanus/acellular pertussis (DTaP) vaccine
  ♦ Encephalopathy within 7 days of DTaP (no other cause apparent)
  ♦ Children with neurological disorders should be evaluated as well
  ♦ Several precautions also exist

• Guillain-Barré Syndrome
  ♦ Intranasal flu
  ♦ Risk vs benefit should be weighed for individuals contemplating IM influenza and DTaP

• Invalid contraindications

- Preterm birth

- Breastfeeding (excluding vaccinia)
- Penicillin allergy
- Duck or feather allergies
- Allergies in blood relatives

- Thimerosal originally identified as causative agent thought to cause autism
  ♦ In July 1999, an agreement was reached that thimerosal should be reduced or eliminated in vaccines as a precautionary measure
  ♦ Additionally, multiple studies have not support a causal link between vaccines (specifically MMR) and autism
  ♦ If still concerned, consult additives and consider using single-use vaccines

➢ Dosing

- Number of doses dependent on vaccine type
  - Live attenuated vaccine
    ♦ First dose:
    ♦ Second dose:
  - Inactivated vaccine
    ♦ Additional boosters may also be needed, dependent on how long individual is at risk for disease

➢ General wisdom about vaccine schedules

- Vaccination only counts as being valid if given up to 4 days prior to minimum interval or age

➢ Interactions

- Immunoglobulin preparations
  - Have no effect on inactivated vaccines
  - Antibody presence decreases immune system response to live attenuated vaccines
  - How to avoid interaction
    ♦ If vaccine given first, wait at least 2 weeks before giving immunoglobulin
    ♦ If immunoglobulin is given first, time period is dependent on vaccine and immunoglobulin, but a three-month interval is at least required

- Other vaccines

- Some vaccines may interact if given on separate days
  ♦ Live attenuated vaccines and intranasal flu vaccines should be separated by at least 4 weeks

- Antibiotics
  - Intranasal flu vaccine
  ♦ Influenza antivirals
  - Varicella
  ♦ Antivirals
  - Oral typhoid
  ♦ Sulfonamides
♦ Other antimicrobials
♦ Should be separate by at least 24 hours

➢ Storage and Reconstitution

- Package insert should be read carefully
  - Refrigerated or frozen?
  - How to reconstitute?

- Do not store dose in syringes
- Do not re-freeze frozen vaccines and discard 30 minutes after reconstitution

❖ Recommended Immunizations

➢ Hepatitis B

- Who?
  - At risk adults
    ♦ Household contacts, sex partners of HBsAg+ persons
    ♦ IVDU
    ♦ Heterosexuals ≥ 1 partner/6 months
    ♦ MSM
    ♦ Recent STD diagnosis
    ♦ HD and patient with renal disease likely to progress to dialysis
    ♦ Receiving certain blood products
    ♦ Healthcare workers, public safety workers
    ♦ Clients, staff of developmentally disabled institutions
    ♦ Inmates in long-term correctional facilities
    ♦ International travelers

- When?
  - **Dose 1**: all newborns prior to discharge

  - **Dose 2**: 1 – 2 months (or at least 4 weeks after Dose 1)
  - **Dose 3**: 6 – 18 months (or at least 8 weeks after Dose 2, 16 weeks after Dose 1)

  If mother is HBsAg+, Dose 1 should be administered within 12 hours of birth in addition to hepatitis B immune globulin
  - No routine need for boosters once complete 3-dose series

➢ Rotavirus

- Who?
  - Infants

  - Caution should be used for
    ♦ Infants with severe acute gastroenteritis
    ♦ Chronic GI disease
    ♦ History of intussusceptions

- When?
  - **Dose 1**: 2 months (may be given as early as 6 weeks)
  - **Dose 2**: 4 months (or at least 4 weeks after Dose 1)
  - **Dose 3**: 6 months (or at least 4 weeks after Dose 2; no later than 32 weeks)

➢ DTaP (Diptheria, Tetanus, acellular Pertussis)

- Who?

  - Which components are given is dependent on age and previous vaccination history

- When?
  - **DTaP**
    ♦ Dose 1: 2 months
    ♦ Dose 2: 4 months (at least 4 weeks after Dose 1)
    ♦ Dose 3: 6 months (at least 4 weeks after Dose 2)
    ♦ Dose 4: 15 – 18 months (at least 6 months after Dose 3)
    ♦ Dose 5: 4 – 6 years
- Do not give if Dose 4 was received at an age older than 4 years old
  - Td, Tdap
    - Booster Tdap
      - 11–12 years if 5 years since DTaP
    - Booster Td
  - Td, Tdap

- Haemophilus influenza type B (Hib)
  - Who?
    - Functional or anatomic asplenia
    - Immunodeficiency
    - Immunosuppression from cancer chemotherapy, HIV, or hematopoietic stem cell transplant
  - When?
    - Should be at least 6 weeks old before Dose 1
    - Dosing dependent on which commercial vaccine is used
      - ActHib
        - Dose 1: 2 months
        - Dose 2: 4 months
        - Dose 3: 6 months
        - Dose 4: 12–15 months
      - PedvaxHIB, Comvax
        - Dose 1: 2 months
        - Dose 2: 4 months
        - Dose 3: 12–15 months
          - If child is behind on vaccinations and is aged 15 months to 5 years, only one dose is required
          - Older children and adults at high risk should receive at least one pediatric dose of any Hib conjugate vaccine

- Pneumococcal Conjugate vaccine (PCV)
  - Provides protection against the 7 serotypes which account for 86% of bacteremia, 83% of meningitis, and 65% of otitis media in children younger than 6 years old (1987-1994)
  - Who?
  - When?
    - Dose 1: 2 months
      - May be given as early as 6 weeks
    - Dose 2: 4 months (at least 4 weeks after Dose 1)
    - Dose 3: 6 months (at least 4 weeks after Dose 2)
    - Dose 4: 12–15 months (at least 8 weeks after Dose 3)
    - If child is behind schedule, number of doses dependent on age
      - 7–11 months: 2 doses, one booster at 12–15 months
      - 12–23 months: 2 doses, at least 8 weeks apart
      - 24–59 months: one dose; consider two doses for children at high risk (i.e. sickle cell, asplenia, HIV, chronic illness, cochlear implant, immunocompromising conditions)

- Inactivated Polio vaccine
  - Who?
  - When?
    - Dose 1:
• Dose 2:
• Dose 3:
• Dose 4: 4 – 6 years (do not need if Dose 3 given at age > 4 years)
• All doses should be separated by at least 4 weeks

➢ Measles, Mumps, Rubella (MMR)
   ▪ Who?
   
   ▪ When?
     • Dose 1: age 12 – 15 months
       ♦ Does NOT count if given prior to 12 months
     • Dose 2: age 4 – 6 years
       ♦ At least 4 weeks from Dose 1 if MMR
       ♦ At least 3 months from Dose 1 if MMRV
     • Certain adults should receive two doses if not previously immunized

➢ Varicella (Chicken pox)
   ▪ Who?
   
     • Any individual 13 years or older without evidence of immunity
       ♦ Especially those at high risk for complications and healthcare personnel
   ▪ When?
     • Dose 1:
     • Dose 2:

     • If exposed to individual with chicken pox, post exposure prophylaxis should be given within 3 to 5 days
   ▪ What?
     • Two possible vaccines
       ♦ Varicella (alone)
       ♦ MMRV (in combination)

➢ Hepatitis A
   ▪ Who?
   
     • Those older than 2 years old who fall into the following categories
       ♦ Routine vaccination program available (areas with greater than 20 cases/ 100,000 people)
       ♦ Travel outside US, Western Europe, Australia, Canada, Japan
       ♦ Chronic liver disease
       ♦ Clotting factor disorder
       ♦ MSM
       ♦ IVDU
       ♦ Experimental laboratory workers
       ♦ Food handlers
   ▪ When?
     • Dose 1:
     • Dose 2:

➢ Neisseria meningitidis; meningococcal vaccine
   ▪ Who?
Asplenia
Terminal complement deficiencies
HIV
Certain genetic factors

Those traveling to endemic areas (e.g. sub-Saharan Africa “meningitis belt”)
Microbiologists working with *N. meningitidis*
Military recruits

**When?**
- Dose 1:

**What?**
- Two different vaccines available with different age recommendations
  - Meningococcal Conjugate vaccine (MCV)
    - Preferred vaccine product
    - Conjugated vaccine product is believed to offer superior immune response
    - Currently recommended product for all individuals requiring immunization ages 2 – 55 years old
  - Meningococcal polysaccharide vaccine (MPSV)
    - Should be limited to persons > 55 years old
    - When MCV is not available

**Human Papillomavirus (HPV)**

**Who?**

- Diagnosis of HPV does not exclude vaccination

**When?**
- Dose 1: 11 – 12 years
- Dose 2: 2 months after Dose 1 (may be shortened to 4 weeks)
- Dose 3: 4 months after Dose 2 (may be shortened to 8 weeks)

**Varicella (Herpes Zoster)**

**Who?**

- ; pneumococcal polysaccharide vaccine (PPV)

  Provides protection 23 strains of *S. pneumoniae* that account for 88% of bacteremic pneumococcal disease

**Who?**

- Chronic cardiac or pulmonary disease
- Alcoholism
- Diabetes
- CSF leak
- Alaska Natives
- Certain American Indian populations
- Asplenia
- Sickle cell
- HIV
- Organ or bone marrow transplant recipient
- Leukemia
- Lymphoma
- Multiple myeloma
- Nephrotic syndrome
- Generalized malignancy
- Immunosuppressive chemotherapy
- Chronic renal failure
- Cochlear implant candidate/recipient

**When?**
- Children
  - Dose 1: 8 weeks after final dose of PCV
  - Dose 2: 3 – 5 years after initial PPV
- Adults
  - Dose 1:
Dose 2:

- Special Vaccine Circumstances
  - Travelers
    - All travelers should be up-to-date with the recommended vaccinations
    - Additional vaccines may be recommended or required, depending on destination
      - Yellow fever
      - Typhoid
      - Japanese encephalitis
      - Rabies
    - For additional information, consult the CDC travel website
  - Health-Care Professionals
    - Recommended vaccines include

- Influenza
  - Background information
    - Viral infection typically seen in late fall and winter (November – May)
    - Two types of viruses capable of causing disease in humans
      - Influenza A (subtypes based on surface proteins)
      - Influenza B (two groups)
    - Two types of changes occur within influenza viruses
      - Antigenic drift:
        - Causes seasonal epidemics
      - Antigenic shift:
        - Causes pandemics
    - Transmission is primarily due to large droplets from respiratory tract of infected individuals but may also be transmitted by inanimate objects that come into contact with these droplets
    - Signs and symptoms usually abrupt and include
      - Fever
      - Myalgia
      - Sore throat
      - Nonproductive cough
      - Headache
    - Typically resolves in 3 – 7 days in normally healthy individuals
    - More severe symptoms, including death, are seen more in the very young (<5 years), very old (≥ 65 years old), and other that are generally not healthy
      - These individuals tend to compromise the majority of those patients who are hospitalized
      - Most people die from bacterial infections secondary to influenza, not the virus itself
  - Prevention Methods
    - The MOST effective way for prevention
      - Frequent hand washing
      - Improved respiratory hygiene
  - Vaccination
    - Vaccines formulated every years based on prediction which strains will be the most prevalent
    - Always contain the same general formulation
      - Influenza A (H3N2)
      - Influenza B (H1N1)
Influenza B

- Two types of flu vaccines
  - Live attenuated: FluMist®
  - Inactivated: Fluarix®, Fluvirin®, Fluzone®, FluLaval®, Alfluria®

- Differences between various flu vaccines
  - All contain same formulation
  - No real difference in efficacy between the live attenuated and inactivated formulations
  - Main difference is FDA approved ages
    - Fluzone: ≥ 6 months
    - Fluvirin: ≥ 4 years
    - Fluarix, FluLaval, Alfluria: ≥ 18 years
    - FluMist: 2 - 49 years
      - Contraindications/Precautions
        - Hypersensitivity to vaccine or eggs
        - Age < 2 years of >50 years
        - Persons with underlying medical conditions that are reasons to receive vaccination
        - Immunodeficiency
        - Children or adolescents on ASA therapy
        - History of Guillain-Barré syndrome
        - Pregnant women
        - History of asthma or recurrent wheezing in the past 12 months for children ages 2 – 4
        - Consider vaccinating another time if significant nasal congestion
        - Household contacts of severely immunosuppressed could theoretically shed virus after vaccination and should be vaccinated with inactivated vaccine

- Who should be vaccinated?
  - Target specifically children 6 months – 4 years in vaccine shortage
  - Children and adolescents on ASA therapy
  - Individuals with
    - COPD
    - Cardiovascular disorders (excluding HTN)
    - Renal disorders
    - Hepatic disorders
    - Hematological disorders
    - Diabetes (or other metabolic disorders)
    - Immunosuppression
    - Conditions that may compromise respiratory function (e.g. seizures, cognitive dysfunction, spinal cord injuries)
  - Nursing home and long-term care facility residents

- Antivirals
  - Two classes of antiviral agents used to treat influenza
    - Neuraminidase inhibitors (oseltamivir (Tamiflu®), zanamivir (Relezna®))
      - MOA:
    - Adamantanes (amantadine (Symmetrel®), rimantidine (Flumadine®))
      - MOA:
- Use of antivirals
  - Prophylaxis
    - Consider using
    - *
    - *
  - Treatment
    - Outpatients
      - Must be started within 48 hours of treatment onset
      - Will reduce illness about 1.5 days
    - Inpatients
      - Oseltamivir may be associated with a mortality reduction in patients hospitalized with influenza
      - Likely underused in this setting
  - Dosing and Adverse Effects

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
<th>Pediatric Dose</th>
<th>Side Effects</th>
<th>Dose adjustment?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir</td>
<td><strong>Tx:</strong> 75 mg BID x 5 days</td>
<td>&lt;15 kg: 30 mg BID</td>
<td>N/V</td>
<td>Renal</td>
</tr>
<tr>
<td></td>
<td><strong>Px:</strong> 75 mg qday &gt; 7 days</td>
<td>15 – 23 kg: 45 mg BID</td>
<td>Bronchitis</td>
<td>CrCL 10 – 30 mL/min: 75 mg qday</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23 – 40 kg: 60 mg BID</td>
<td>Insomnia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>&gt; 40 kg: 75 mg BID</td>
<td>Vertigo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration: 5 days</td>
<td>Neuropsychiatric events (rare)</td>
<td></td>
</tr>
<tr>
<td>Zanamivir</td>
<td>10 mg (2 inhalations) BID x 5 days</td>
<td>Age ≥ 7 years: 10 mg (2 inhalations) BID x 5 days</td>
<td>Sinusitis Dizziness Fever/chills Bronchospasm (rare)</td>
<td>None</td>
</tr>
</tbody>
</table>

- Resources
  - The Pink Book (Epidemiology and Prevention of Vaccine-Preventable Diseases)
    - Updated yearly
    - Available at [http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm](http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm)
  - The Yellow Book (CDC Health Information for International Travel)
    - Updated every two years
    - Available at [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm)